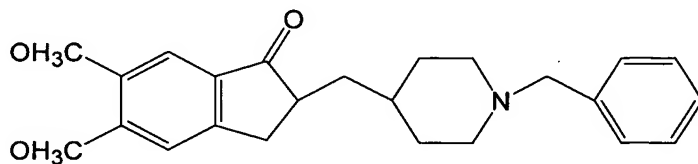


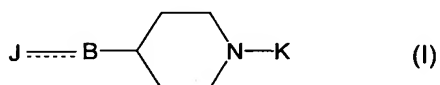
## CLAIMS

1. A protective agent for neurons of the central nervous system, comprising any one of the compounds shown in the following (i) to (vii):

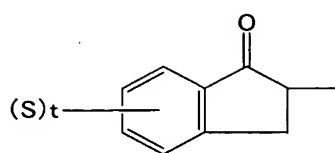
- 5            (i) 1-benzyl-4-[(5,6-dimethoxy-1-indanone)-2-yl]methylpiperidine represented by the following chemical formula or a pharmacologically acceptable salt thereof:



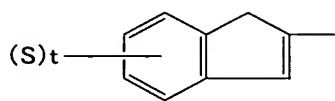
- 10           (ii) a cyclic amine derivative represented by the following general formula (I) or a pharmacologically acceptable salt thereof:



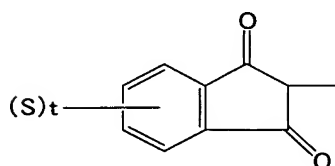
- 15           where J is a monovalent or divalent group selected from the groups represented by the following formulas:



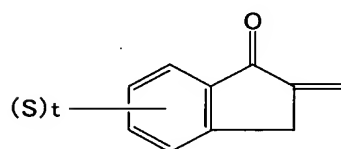
Indanonyl



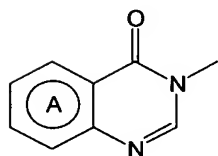
Indenyl



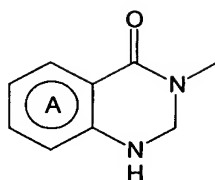
Indandionyl



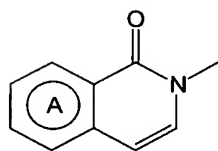
Indanolydenyl



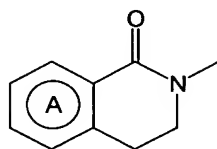
(a)



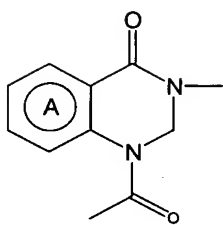
(b)



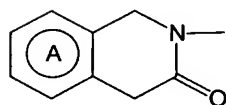
(c)



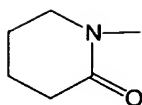
(d)



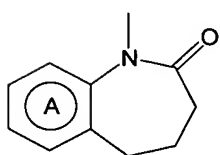
(e)



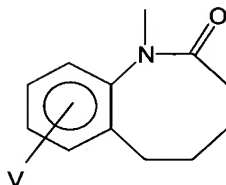
(g)



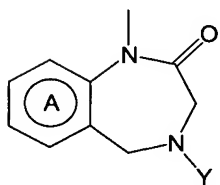
(h)



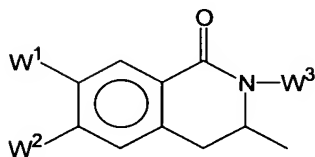
(j)



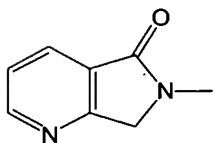
(k)



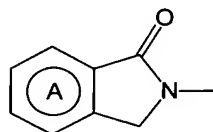
(l)



(n)



(p)



(q)

5

where S is a lower alkyl group with 1 to 6 carbon atoms, a lower alkoxy group with 1 to 6 carbon groups, a halogen atom or a hydroxyl group; t is 0 or an integer from 1 to

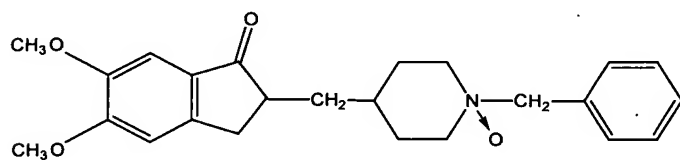
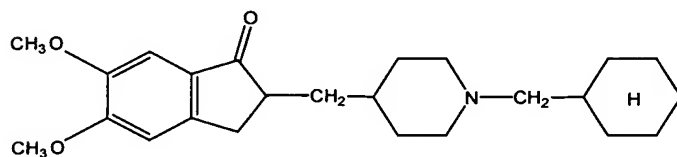
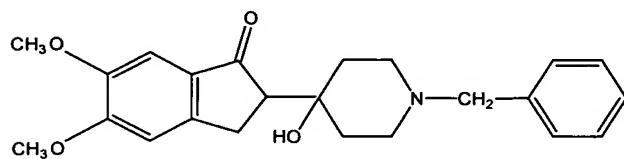
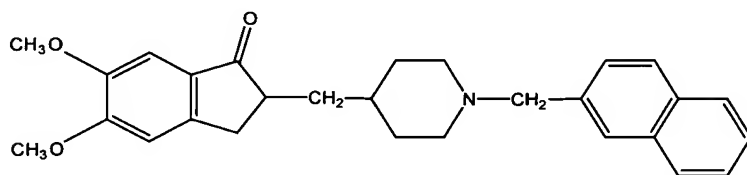
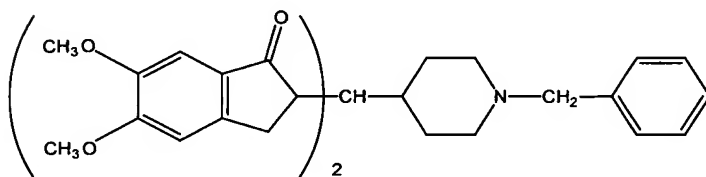
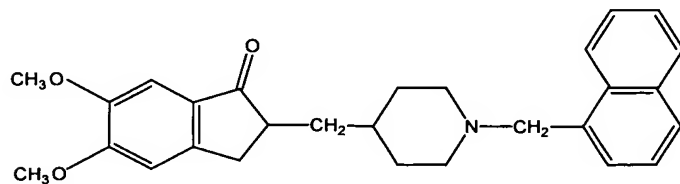
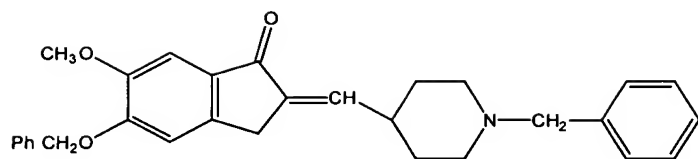
4; (S)<sub>t</sub> may form a methylenedioxy or ethylenedioxy group between adjacent carbon atoms on the phenyl ring linked; Y in formula (l) is a hydrogen atom or a lower alkyl group with 1 to 6 carbon atoms; V in formula (k) is a hydrogen atom or a lower alkoxy group with 1 to 6 carbon atoms; W<sup>1</sup> and W<sup>2</sup> in formula (n) independently represent, similarly or differently, a hydrogen atom, a lower alkyl group with 1 to 6 carbon atoms, or a lower alkoxy group with 1 to 6 carbon atoms; W<sup>3</sup> in formula (n) is a hydrogen atom or a lower alkyl group with 1 to 6 carbon atoms; phenyl ring A in formulas (a) to (e), (g), (j), (l) and (q) may be substituted with an alkyl group with 1 to 6 carbon atoms or a alkoxy group with 1 to 6 carbon atoms;

B is a group represented by a formula  $-(CHR^2)_n-$  (where n is 0 or an integer from 1 to 10; R<sup>2</sup> is each independently a hydrogen atom or a methyl group), a group represented by a formula  $=(CH-CH=CH)_b-$  (where b is an integer from 1 to 3), a group represented by a formula  $=CH-(CH_2)_c-$  (where c is 0 or an integer from 1 to 9), or a group represented by a formula  $=(CH-CH)_d=$  (where d is 0 or an integer from 1 to 5);

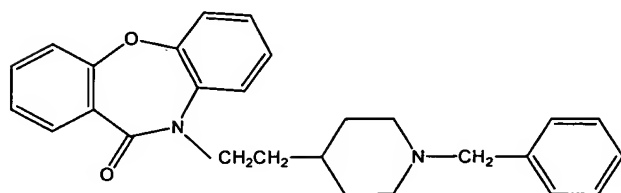
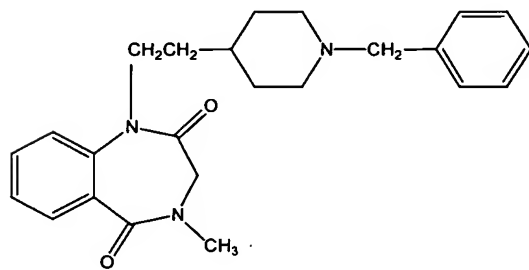
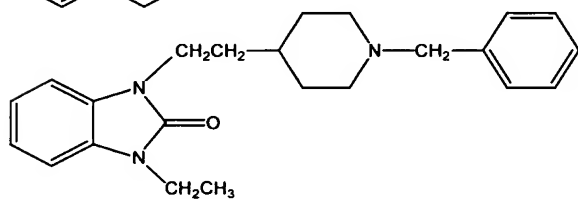
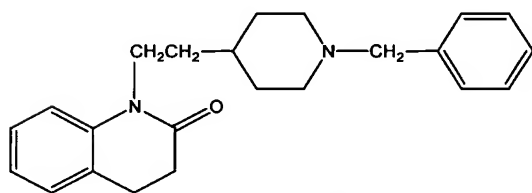
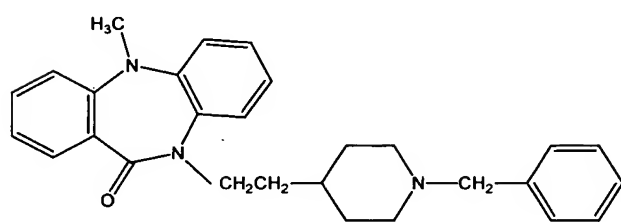
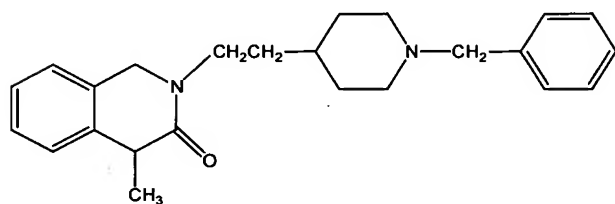
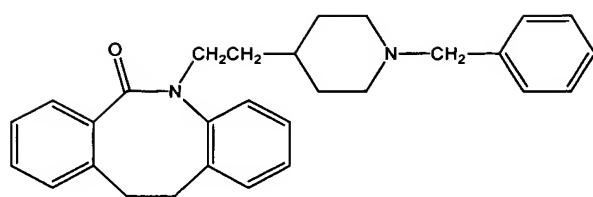
K is a phenylalkyl group that may have, as a substituent, an alkyl group with 1 to 6 carbon atoms which may be halogenated, an alkoxy group with 1 to 6 carbon atoms, a nitro group, a halogen atom, a carboxyl group, a benzyloxy group, an alkoxycarbonyl group with 1 to 6 carbon atoms, an amino group, a monoalkylamino group with 1 to 6 carbon atoms, a dialkylamino group with 1 to 6 carbon atoms, a carbamoyl group, an acylamino group with 1 to 6 carbon atoms, a cyclohexyloxycarbonyl group, an alkylaminocarbonyl group with 1 to 6 carbon atoms, an alkylcarbonyloxy group with 1 to 6 carbon atoms, a hydroxyl group, a formyl group or an alkoxy (with 1 to 6 carbon atoms)-alkyl (with 1 to 6 carbon atoms) group; and

==== represents a single bond or a double bond;

(iii) a cyclic amine derivative selected from the compounds represented by the following formulas or a pharmacologically acceptable salt thereof:



(iv) a cyclic amine derivative selected from the compounds represented by the following formulas or a pharmacologically acceptable salt thereof:





a quinolyl group; a quinoxalyl group; a furyl group or a group represented by a formula  $R^1-CH=CH-$  (where  $R^1$  is a hydrogen atom or a lower alkoxy carbonyl group);

B is a group represented by a formula  $-(CH_2)_n-$ , a group represented by a formula  $-NR^2-(CH_2)_n-$  (where  $R^2$  is a hydrogen atom, a lower alkyl group, a phenyl group or a lower alkylsulfonyl group), a group represented by a formula  $-CONR^3-(CH_2)_n-$  (where  $R^3$  is a hydrogen atom, a lower alkyl group, a phenyl, benzyl or pyridyl group which may have, as a substituent, a lower alkyl group, a lower alkoxy group, a halogen or a hydroxyl group), a group represented by a formula  $-NH-CO-(CH_2)_n-$ , a group represented by a formula  $-CH_2-CO-NH-(CH_2)_n-$ , a group represented by a formula  $-CO-CH_2-CH(OH)-CH_2-$ , a group represented by a formula  $-CO-(CH_2)_n-$ , a group represented by a formula  $-C(OH)-(CH_2)_n-$  or a group represented by a formula  $-CO-CH=CH-CH_2-$ ; and n in the above formulas is 0 or an integer from 1 to 10;

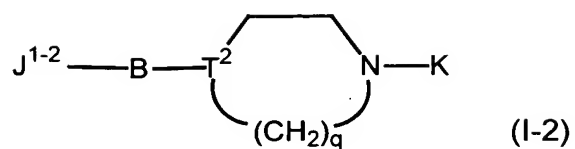
$T^1$  is a carbon atom;

K is a phenylalkyl group (where the alkyl has 1 to 2 carbon atoms) in which the phenyl may have, as a substituent, a lower alkyl group, a lower alkoxy group, a nitro group, a halogen, a carboxyl group, a lower alkoxy carbonyl group, an amino group, a mono-lower alkylamino group, a di-lower alkylamino group, a carbamoyl group, an acylamino group derived from aliphatic saturated monocarboxylic acid with 1 to 6 carbon atoms, a cyclohexyloxy carbonyl group, a lower alkylaminocarbonyl group, a lower alkylcarbonyloxy group, a halogenated lower alkyl group, a hydroxyl group, a formyl group or a lower-alkoxy-lower-alkyl group; a cinnamyl group; a lower alkyl group; a pyridyl methyl group; a cycloalkyl (with 3 to 6 carbon atoms)-alkyl group; an adamantanemethyl group; a furfuryl group; a cycloalkyl group with 3 to 6 carbon atoms; or an acyl group; and

q is 1 or 2;

(vi) a cyclic amine derivative represented by the following general formula (I-2) or a pharmacologically acceptable salt thereof:

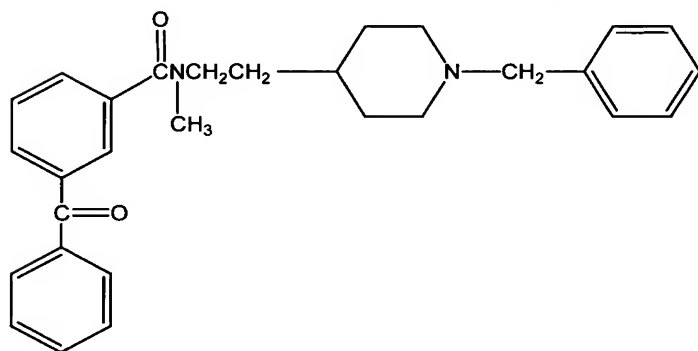
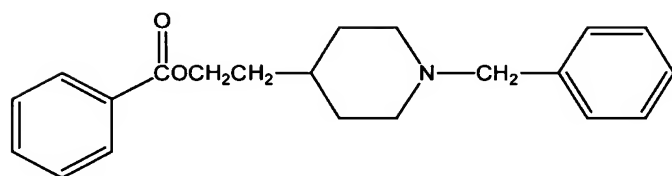
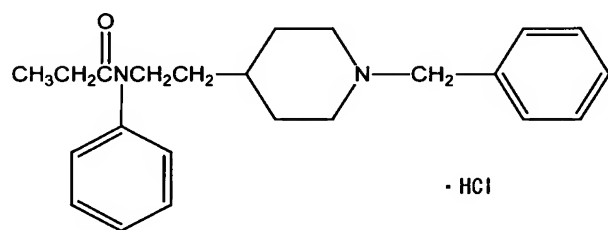
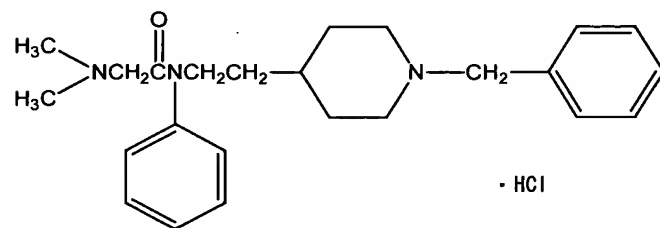
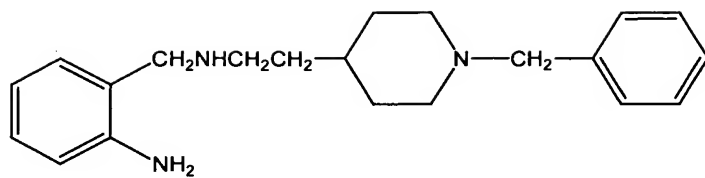


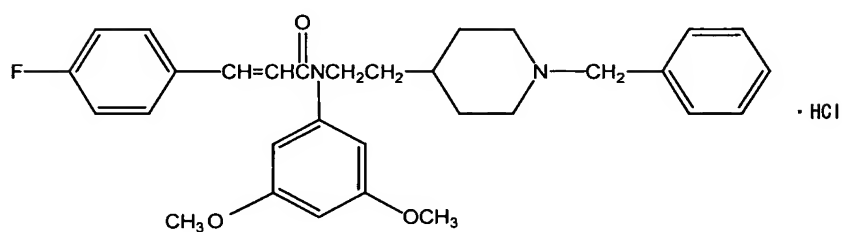
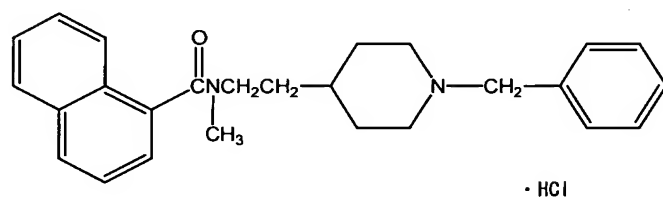
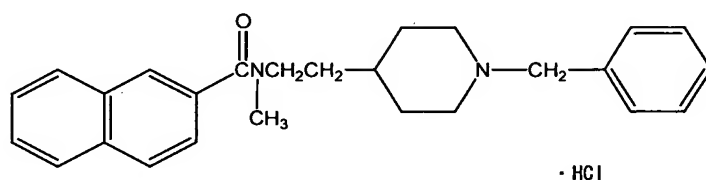
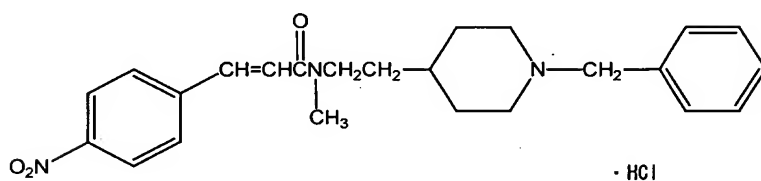
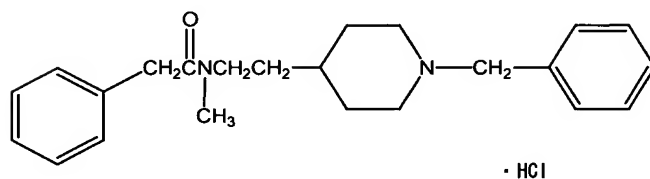
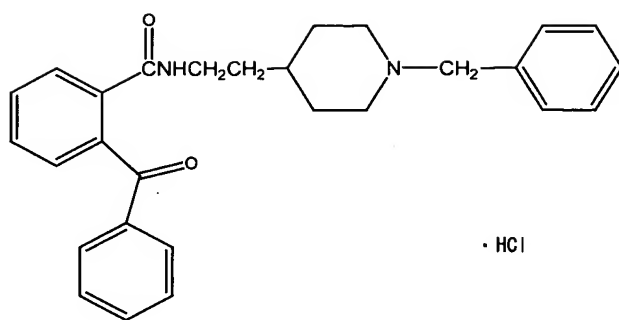


where  $J^{1-2}$  is an indanonyl group which may have, as a substituent, a lower alkyl group with 1 to 6 carbon atoms or a lower alkoxy group with 1 to 6 carbon atoms;  $T^2$  is a nitrogen atom; B, K and q are the same as defined above;

5

(vii) a cyclic amine derivative selected from the compounds represented by the following formulas or a pharmacologically acceptable salt thereof:



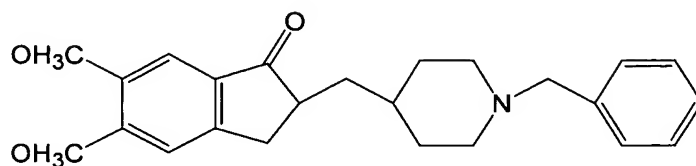


2. The protective agent according to claim 1, wherein the salt is a hydrochloride salt.

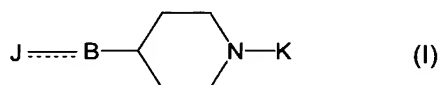
5 3. A prophylactic and/or therapeutic agent for disorders in neurons of the central nervous system, comprising any one of the compounds shown in the following (i) to (vii):

(i) 1-benzyl-4-[(5,6-dimethoxy-1-indanone)-2-yl]methylpiperidine represented by

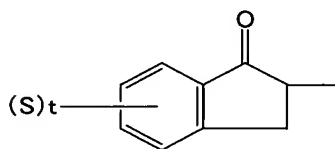
the following chemical formula or a pharmacologically acceptable salt thereof:



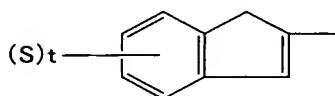
- 5 (ii) a cyclic amine derivative represented by the following general formula (I) or a pharmacologically acceptable salt thereof:



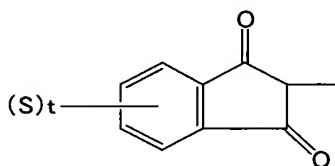
where J is a monovalent or divalent group selected from the groups represented by the following formulas:



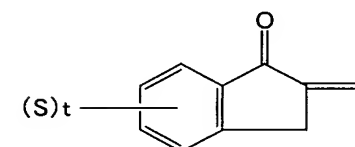
Indanonyl



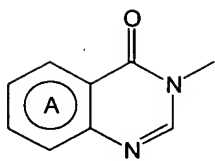
Indenyl



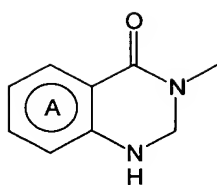
Indandionyl



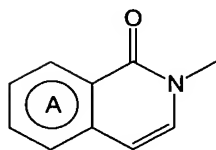
Indanolydenyl



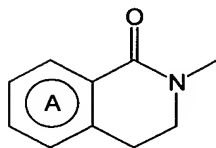
(a)



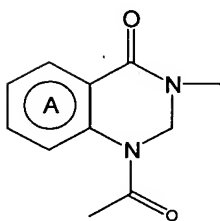
(b)



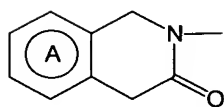
(c)



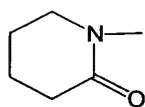
(d)



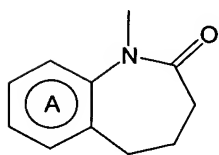
(e)



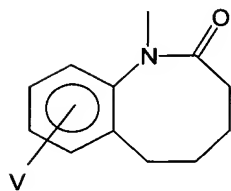
(g)



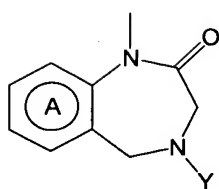
(h)



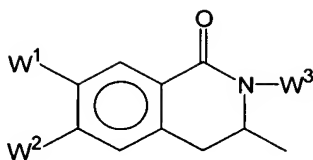
(j)



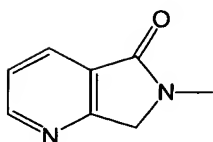
(k)



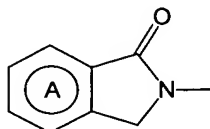
(l)



(n)



(p)



(q)

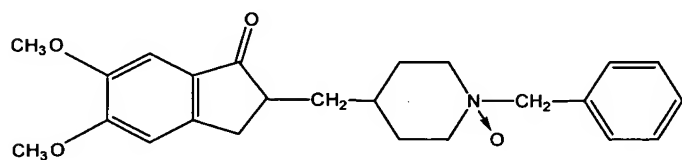
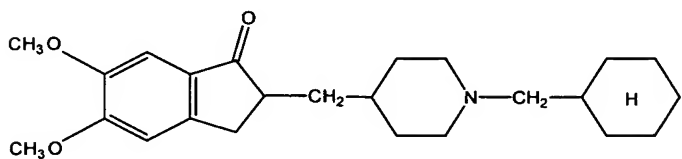
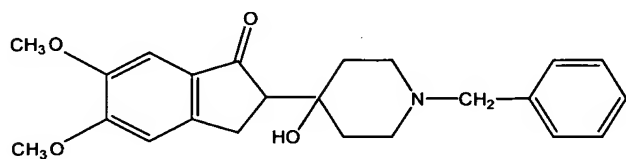
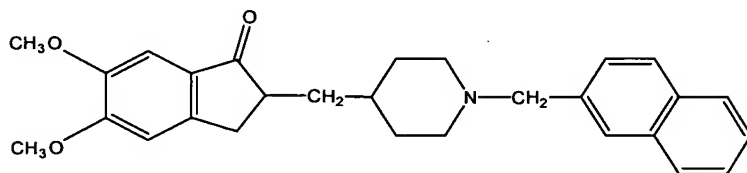
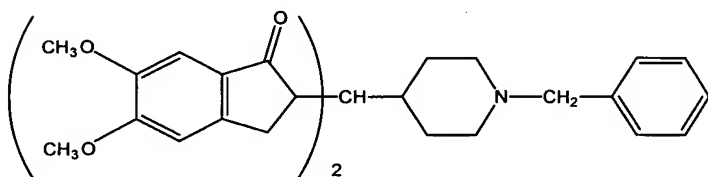
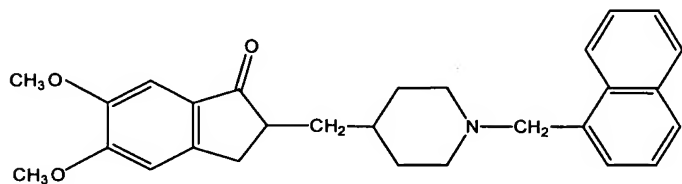
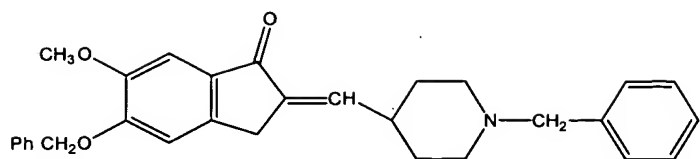
where S is a lower alkyl group with 1 to 6 carbon atoms, a lower alkoxy group with 1 to 6 carbon groups, a halogen atom or a hydroxyl group; t is 0 or an integer from 1 to 4; (S)<sub>t</sub> may form a methylenedioxy or ethylenedioxy group between adjacent carbon atoms on the phenyl ring linked; Y in formula (l) is a hydrogen atom or a lower alkyl group with 1 to 6 carbon atoms; V in formula (k) is a hydrogen atom or a lower alkoxy group with 1 to 6 carbon atoms; W<sup>1</sup> and W<sup>2</sup> in formula (n) independently represent, similarly or differently, a hydrogen atom, a lower alkyl group with 1 to 6 carbon atoms, or a lower alkoxy group with 1 to 6 carbon atoms; W<sup>3</sup> in formula (n) is a hydrogen atom or a lower alkyl group with 1 to 6 carbon atoms; phenyl ring A in formulas (a) to (e), (g), (j), (l) and (q) may be substituted with an alkyl group with 1 to 6 carbon atoms or a alkoxy group with 1 to 6 carbon atoms;

B is a group represented by a formula  $-(\text{CHR}^2)_n-$  (where n is 0 or an integer from 1 to 10; R<sup>2</sup> is each independently a hydrogen atom or a methyl group), a group represented by a formula  $=(\text{CH}-\text{CH}=\text{CH})_b-$  (where b is an integer from 1 to 3), a group represented by a formula  $=\text{CH}-(\text{CH}_2)_c-$  (where c is 0 or an integer from 1 to 9), or a group represented by a formula  $=(\text{CH}-\text{CH})_d=$  (where d is 0 or an integer from 1 to 5);

K is a phenylalkyl group that may have, as a substituent, an alkyl group with 1 to 6 carbon atoms which may be halogenated, an alkoxy group with 1 to 6 carbon atoms, a nitro group, a halogen atom, a carboxyl group, a benzyloxy group, an alkoxy carbonyl

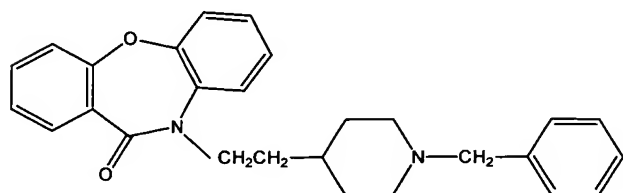
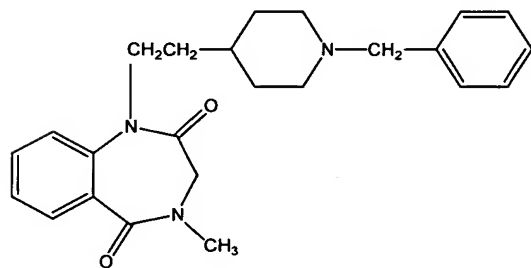
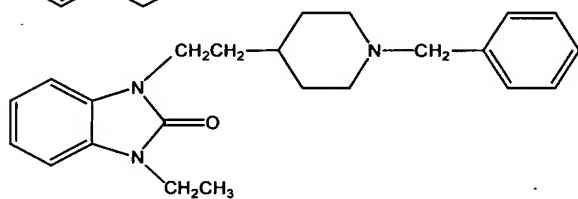
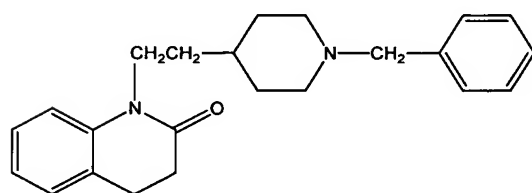
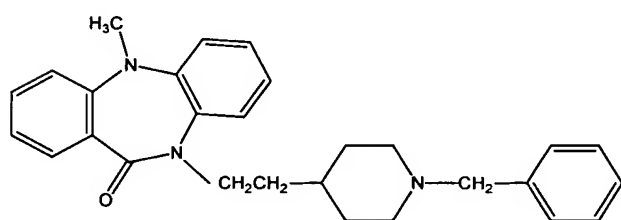
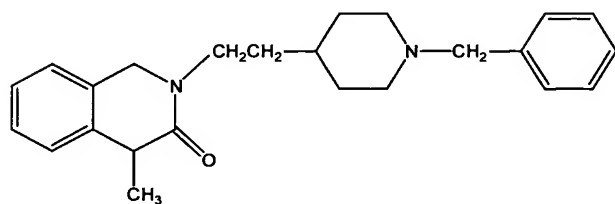
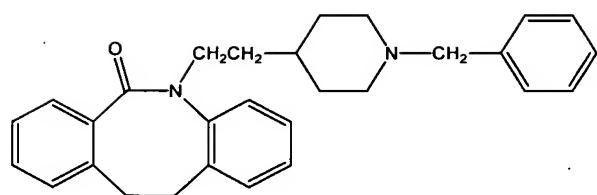
group with 1 to 6 carbon atoms, an amino group, a monoalkylamino group with 1 to 6 carbon atoms, a dialkylamino group with 1 to 6 carbon atoms, a carbamoyl group, an acylamino group with 1 to 6 carbon atoms, a cyclohexyloxycarbonyl group, an alkylaminocarbonyl group with 1 to 6 carbon atoms, an alkylcarbonyloxy group with 1 to 6 carbon atoms, a hydroxyl group, a formyl group or an alkoxy (with 1 to 6 carbon atoms)-alkyl (with 1 to 6 carbon atoms) group; and  
----- represents a single bond or a double bond;

(iii) a cyclic amine derivative selected from the compounds represented by the following formulas or a pharmacologically acceptable salt thereof:

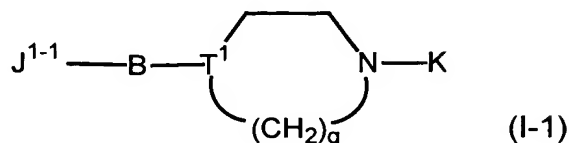


(iv) a cyclic amine derivative selected from the compounds represented by the following formulas or a pharmacologically acceptable salt thereof:

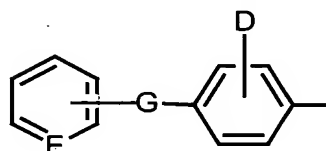




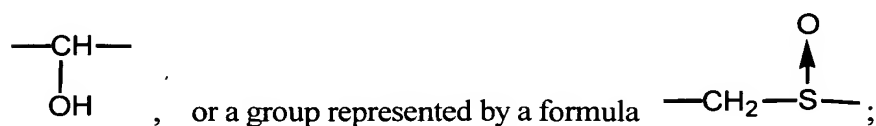
(v) a cyclic amine derivative represented by the following general formula (I-1) or a pharmacologically acceptable salt thereof:



5 where J<sup>1-1</sup> is a lower alkyl group with 1 to 6 carbon atoms (hereinafter, just referred to as "lower alkyl group"); a cyclohexyl group; a phenyl, pyridyl or pyrazyl group which may have, as a substituent, a lower alkyl group, a lower alkoxy group with 1 to 6 carbon atoms (hereinafter, just referred to as "lower alkoxy group"), a nitro group, a  
10 halogen, a carboxyl group, a lower alkoxy carbonyl group, an amino group, a mono-lower alkylamino group, a di-lower alkylamino group, a carbamoyl group, an acylamino group derived from aliphatic saturated monocarboxylic acid with 1 to 6 carbon atoms, a cyclohexyloxy carbonyl group, a lower alkylaminocarbonyl group, a lower alkylcarbonyloxy group, a halogenated lower alkyl group, a hydroxyl group, a  
15 formyl group or a lower-alkoxy-lower-alkyl group; a group represented by a formula



where G is a group represented by a formula  $\text{—}\overset{\text{O}}{\parallel}{\text{C}}\text{—}$ , a group represented by a  
formula  $\text{—}\overset{\text{O}}{\parallel}{\text{C}}\text{—}$ , a group represented by a formula  $\text{—O—}$ , a group represented  
by a formula  $\text{—CH}_2\text{—NH—}\overset{\text{O}}{\parallel}{\text{C}}\text{—}$ , a group represented by a formula  $\text{—CH}_2\text{—O—}$ , a  
20 group represented by a formula  $\text{—CH}_2\text{—SO}_2\text{—}$ , a group represented by a formula



E is a carbon atom or a nitrogen atom;

a quinolyl group; a quinoxalyl group; a furyl group or a group represented by a formula  $R^1\text{-CH=CH-}$  (where  $R^1$  is a hydrogen atom or a lower alkoxy carbonyl group);

B is a group represented by a formula  $\text{-(CH}_2\text{)}_n\text{-}$ , a group represented by a formula  $\text{-NR}^2\text{-(CH}_2\text{)}_n\text{-}$  (where  $R^2$  is a hydrogen atom, a lower alkyl group, a phenyl group or a lower alkylsulfonyl group), a group represented by a formula  $\text{-CONR}^3\text{-(CH}_2\text{)}_n\text{-}$  (where  $R^3$  is a hydrogen atom, a lower alkyl group, a phenyl, benzyl or pyridyl group which may have, as a substituent, a lower alkyl group, a lower alkoxy group, a halogen or a hydroxyl group), a group represented by a formula  $\text{-NH-CO-(CH}_2\text{)}_n\text{-}$ , a group represented by a formula  $\text{-CH}_2\text{-CO-NH-(CH}_2\text{)}_n\text{-}$ , a group represented by a formula  $\text{-CO-CH}_2\text{-CH(OH)-CH}_2\text{-}$ , a group represented by a formula  $\text{-CO-(CH}_2\text{)}_n\text{-}$ , a group represented by a formula  $\text{-C(OH)-(CH}_2\text{)}_n\text{-}$  or a group represented by a formula  $\text{-CO-CH=CH-CH}_2\text{-}$ ; and  $n$  in the above formulas is 0 or an integer from 1 to 10;

$T^1$  is a carbon atom;

K is a phenylalkyl group (where the alkyl has 1 to 2 carbon atoms) in which the phenyl may have, as a substituent, a lower alkyl group, a lower alkoxy group, a nitro group, a halogen, a carboxyl group, a lower alkoxy carbonyl group, an amino group, a mono-lower alkylamino group, a di-lower alkylamino group, a carbamoyl group, an acylamino group derived from aliphatic saturated monocarboxylic acid with 1 to 6 carbon atoms, a cyclohexyloxy carbonyl group, a lower alkylaminocarbonyl group, a lower alkylcarbonyloxy group, a halogenated lower alkyl group, a hydroxyl group, a formyl group or a lower-alkoxy-lower-alkyl group; a cinnamyl group; a lower alkyl group; a pyridyl methyl group; a cycloalkyl (with 3 to 6 carbon atoms)-alkyl group; an adamantanemethyl group; a furfuryl group; a cycloalkyl group with 3 to 6 carbon atoms; or an acyl group; and

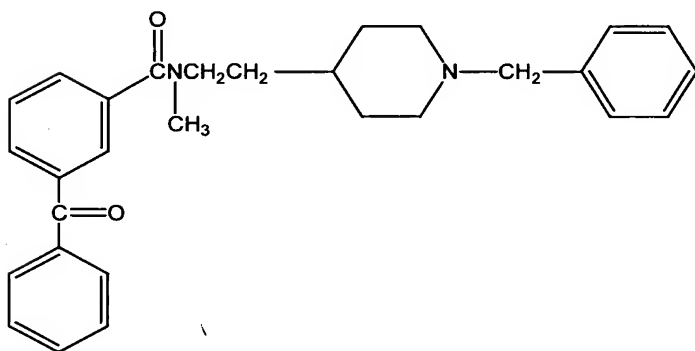
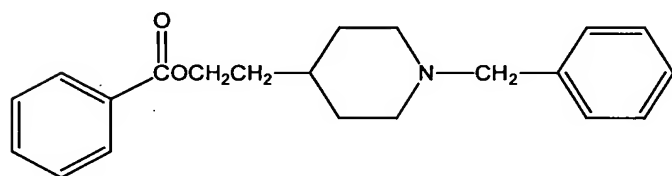
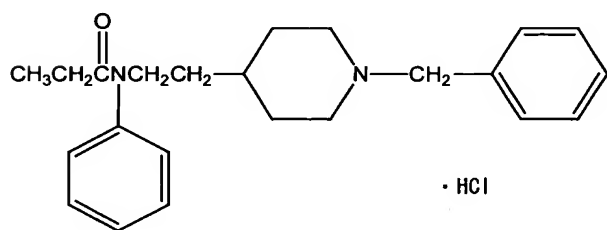
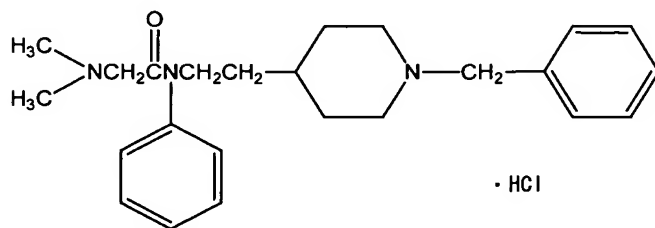
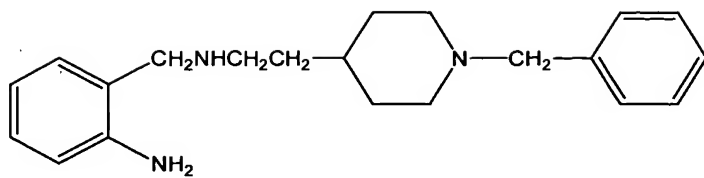
$q$  is 1 or 2;

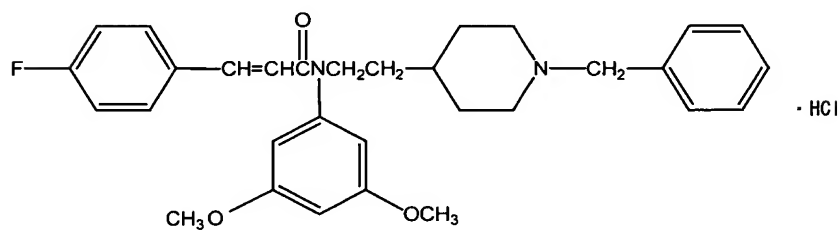
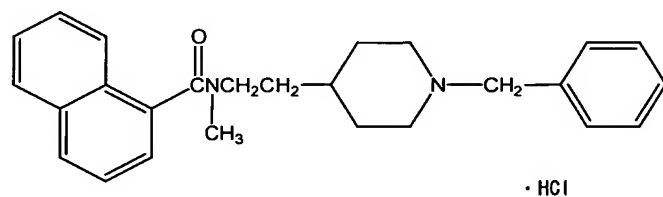
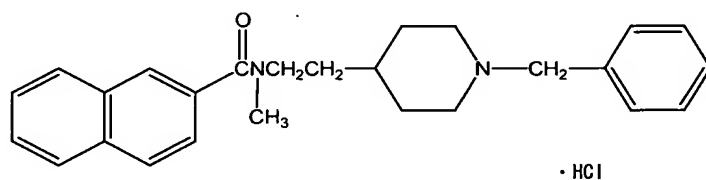
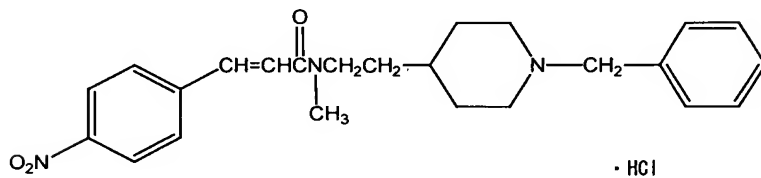
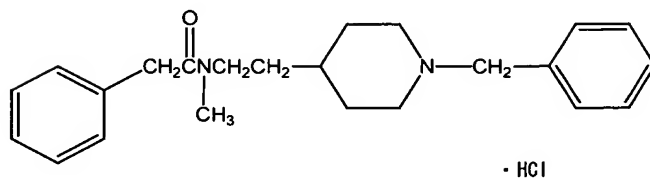
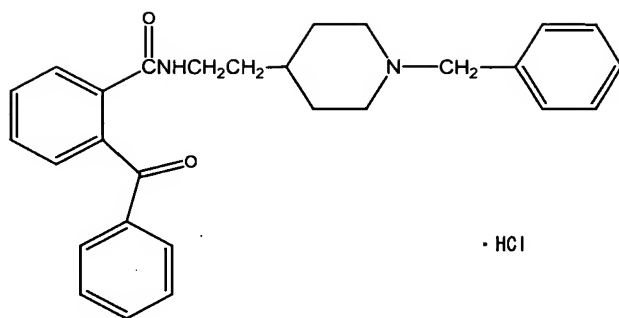
(vi) a cyclic amine derivative represented by the following general formula (I-2) or a pharmacologically acceptable salt thereof:



5

80





4. The prophylactic and/or therapeutic agent according to claim 3, wherein the salt is a hydrochloride salt.

5

5. The prophylactic and/or therapeutic agent according to claim 3 or 4, wherein the neurocyte disorder is induced by cerebral ischemia, excitotoxicity or A $\beta$  toxicity.

6. The prophylactic and/or therapeutic agent according to claim 3 or 4, wherein the neurocyte disorder is induced by cerebral ischemia or excitotoxicity associated with any one of cerebral apoplexy, cerebral infarction or cerebral embolism.
- 5
7. The prophylactic and/or therapeutic agent according to claim 6, wherein the excitotoxicity is by NMDA or kainic acid.
8. The prophylactic and/or therapeutic agent according to claim 3 or 4, wherein the neurocyte disorder is induced by A $\beta$  toxicity associated with Alzheimer's disease or Down's syndrome.
- 10
9. The agent according to any one of claims 1 to 8, wherein the neurons are brain-derived, mature neurons.
- 15
10. The agent according to claim 9, wherein the neurons are derived from any one of cerebral cortex, septal area or hippocampus.
11. The agent according to claim 9 or 10, wherein the neurons are primary culture cells.
- 20
12. A prognosis improving agent for any disease selected from cerebral apoplexy, cerebral infarction or cerebral embolism, comprising the protective agent according to claim 1 or 2 or the prophylactic and/or therapeutic agent according to claim 3 or 4.
13. A method of protecting neurons of the central nervous system, comprising administering to a patient an effective amount of the protective agent according to claim 1 or 2.
- 25
14. A method of preventing and/or treating disorders in neurons of the central nervous system, comprising administering to a patient an effective amount of the prophylactic and/or therapeutic agent according to claim 3 or 4.
- 30
15. The method according to claim 14, wherein the disorder in neurons of the central nervous system is induced by cerebral ischemia, excitotoxicity or A $\beta$  toxicity.
16. The method according to claim 15, wherein the excitotoxicity is induced by NMDA or

kainic acid.

17. The method according to claim 14, wherein the disorder in neurons of the central nervous system is induced by cerebral ischemia or excitotoxicity associated with any one of cerebral apoplexy, cerebral infarction or cerebral embolism.
18. The method according to claim 14, wherein the disorder in neurons of the central nervous system is induced by A $\beta$  toxicity associated with Alzheimer's disease or Down's syndrome.
19. A method of improving the prognosis of any one of cerebral apoplexy, cerebral infarction or cerebral embolism, comprising administering to a patient an effective amount of the prognosis improving agent according to claim 12.
20. Use of any one of the compounds shown in claim 1 or 2 for preparing any agent selected from the group consisting of the protective agent according to claim 1 or 2, the prophylactic and/or therapeutic agent according to any one of claims 3 to 8, and the prognosis improving agent according to claim 12.
21. A method of screening for a compound with A $\beta$  aggregation inhibitory effect or a pharmacologically acceptable salt thereof, comprising contacting cholinergic neurons of the central nervous system with a candidate compound in the presence of A $\beta$  and detecting or measuring the amount of A $\beta$  aggregation.
22. The method according to claim 21, wherein the results of detection or measurement of the amount of A $\beta$  aggregation are compared with the amount of A $\beta$  aggregation in the absence of the candidate compound to thereby judge whether or not the candidate compound has A $\beta$  aggregation inhibitory effect.
23. A screening kit for a compound with A $\beta$  aggregation inhibitory effect or a pharmacologically acceptable salt thereof, which is for use in the method according to claim 21 or 22.
24. A method for screening for a compound, or a pharmacologically acceptable salt thereof, effective for preventing and/or treating disorders in neurons of the central nervous system



induced by A $\beta$  toxicity, comprising contacting cholinergic neurons of the central nervous system with a candidate compound in the presence of A $\beta$  and detecting cytotoxicity or cell death.

- 5     25. The method according to claim 24, wherein the results of detection of cytotoxicity or cell death are compared with the extent of cytotoxicity or cell death in the absence of the candidate compound to thereby judge whether or not the candidate compound has cell protective effect against A $\beta$  toxicity.
- 10    26. The method according to claim 24 or 25, wherein the detection of cytotoxicity or cell death is performed by measuring the concentration of lactate dehydrogenase or by MTT assay.
- 15    27. A screening kit for a compound, or a pharmacologically acceptable salt thereof, effective for preventing and/or treating disorders in neurons of the central nervous system induced by A $\beta$  toxicity, which is for use in the method according to claim 24 or 25.